REMARKS AND ARGUMENTS

Amendment to the Claims

Claims 2-26, 39, 40, 46, and 47 were previously canceled without prejudice. Claim 38 is canceled herein without prejudice. Claims 41 and 48-52 have been amended to correct claim dependencies. Claims 56-66 are new. The support for new claims can be found in the claims as originally filed. No new matter has been added by way of these amendments. Claims 1, 27-37, 41-45, and 48-66 are now pending.

Obviousness-Type Double Patenting Rejection

Claims 38, 41-45, 48-51, 54, and 55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1 and 28-49 of co-pending Application Serial No. 10/493,582 ("the '582 application". Claim 38 has been canceled, thus rendering the rejection moot as to this claim.

Applicant respectfully submits that claims 41-45, 48-51, 54, and 55 are patentably distinct from claims 1 and 28-49 of the '582 application and requests withdrawal of the rejection. Alternatively, Applicant respectfully submits that that the provisional rejection should be held in abeyance until the application is otherwise deemed allowable. To that end, Applicant understands that Examiner will withdraw the provisional double-patenting rejection at that time to permit the application to issue as a patent. MPEP 804(I)(B). Furthermore, Applicant reserves the right to address the merits of the provisional rejection and, without acceding to the merits of the rejection, Applicant will consider filing a terminal disclaimer upon notice of an allowable claim in the instant application and at such time that the '582 application issues as a patent.

Claim Objections

Claim 38 is objected to because of certain informalities. Applicant respectfully submits that claim 38 has been canceled, thus obviating this objection. Accordingly, Applicant respectfully request withdrawal of the objection.

35 USC § 103 Rejections

Claims 38, 41, 42, 45, 48-51, 54 and 55 stand rejected under 35 USC §103(a) as being allegedly obvious over Shibata *et al.* (EP 0989136) ("Shibata"), Noaln *et al.* (WO 97/27212) ("Noaln"), Daniels *et al.* (J. Mol. Biol. Vol. 243:639-652; 1994) ("Daniels"), and

if necessary, in view of Tenson *et al.* (J. Biol. Chem. Vol. 272(28): 17425-17430) ("Tenson"). Applicant respectfully traverses this rejection.

As the preliminary matter, Applicant respectfully submits that claim 38 has been canceled, thus rendering the rejection moot as to this claim.

The Office assert on page 10 of the Office Action that a person of ordinary skill in the art would have been motivated at the time of the invention to use a library of peptides of small length such as 3 to 6 amino acids, because Daniel teaches the need to identify small peptides that can interact with p53. In addition, the Office asserts that because Shibata, Daniel, and Tenson teach methods of using/screening peptide libraries having various length, it would have been obvious to one skilled in the art to substitute longer peptides (> 15 amino acids) for shorter peptides (3-6 amino acids) to achieve the predictable result of screening/using peptide libraries to identify peptides based on the purpose of the experimental design. Based on that, the Office concludes that a *prima facie* case of obviousness has been established. Applicants respectfully disagree.

At the onset it should be appreciated that instant claims are directed to a method of identifying a peptide of 2-8 amino acids in length having the ability to restore the function of p53 in an intra-cellular environment. Furthermore, the instant claims disclose a step of screening a library and a step of identifying the peptide which has been found to restore the function of p53. Yet further, fundamentally, a library of peptides by definition refers to a collection of peptides of unknown sequence; thus, the identity of the peptide in the method of the instant claims is only determined after a library has been screened.

In contrast, Shibata generally teaches methods of individually administering peptides of known sequence (*see* Examples 1-14, pp. 24-30) to host cells to determine whether they modify the activity of p53 (*see e.g.,* Test Example 2, pp. 18-19). Thus, unlike the instant claims, Shibata does not teach a method in which a library of peptides of unknown sequences is screened to identify a peptide capable of restoring function of p53.

Moreover, Shibata teaches that peptides capable of restoring p53 activity need to have specific features (*see* Abstract), with preferred peptides being identified in Tables 1-1 and 1-2. The exemplified compounds are all cyclic peptides of at least 11 amino acids in length. Thus, Shibata is totally silent on that much smaller peptides, namely

peptides of 2 to 8 amino acids in length, could be useful in restoring or modifying the function of p53 (*see also*, page 8 of the Office Action mailed March 23, 2010).

Shibata provides no reason to the one skilled in the art to use peptides of 2 to 8 amino acids in a method of the instant claims with a reasonable expectation that these peptides would be capable of restoring or modifying the function of p53. The results achieved by the present inventors (i.e., identifying peptides of 2 to 8 amino acids in length having the ability to restore the function of p53 in an intra-cellular environment) were not reasonably predictable from Shibata. Without a reason to use these peptides in the presently claimed method nor predictability that peptides of 2 to 8 amino acids in length would be effective in restoring the function of p53 in an intra-cellular environment, the presently claimed method cannot be obvious. *KSR Int'l Co. v. Teleflex Inc.*, 127 U.S. 1727 (2007).

The teachings of Noaln do not cure the deficiencies of Shibata. Noaln generally teaches making and using peptide libraries in target screening assays (*see* Abstract). Furthermore, Noaln teaches that screening assays could be used to identify peptides that can "reactivate" or "compensate" for p53 activity, especially in tumor cells (*see e.g.*, p. 37, ll. 25+; *see also*, p. 9 of the Office Action). However, Noaln is silent on identifying peptides of 2-8 amino acids in length having the ability to restore the function of p53 in an intra-cellular environment.

The Office asserts on page 9 of the Office Action that Noaln teaches peptides with various lengths such as 9 amino acids (see p. 22, ll. 15+). However, disclosure of a peptide of 9 amino acids does not in any way teach or suggest peptides of 2-8 amino acids. Indeed, Noaln teaches away from the use of peptides having 2-8 amino acids in length, because Noaln discloses that peptides within peptide libraries used in target screening assays should incorporate a randomized sequence of 9 amino acids. Thus, based on Noaln, the one skilled in the art would not be motivated to use peptides of 2-8 amino acids in length in the method of instant claims.

The teachings of Daniels also do not cure the deficiencies of Shibata. Daniels generally teaches the use of phage display libraries to identify peptides that bind to p53 (*see e.g.*, Abstract). However, Daniels is silent on identifying peptides of 2-8 amino acids in length having the ability to restore the function of mutant p53 in an intra-cellular environment. In fact, Daniels teaches that peptides which recognize and bind wild-type conformation of p53 are much less likely to recognize a mutant conformation of p53 (see

p. 645, column 2, last paragraph). In contrast, the instant claims are directed to a method of identifying a peptide of 2-8 amino acids in length having the ability to restore the function of wild-type and/or mutant p53 in an intra-cellular environment (*see e.g.*, Specification, p. 6, ll. 25-35, p. 8, ll. 20-35).

Furthermore, the teachings of Tenson also do not cure the deficiencies of Shibata. Tenson generally discloses peptides that can confer erythromycin resistance. This is completely different field from the field of the present invention. One skilled in the art would not be motivated to replace the peptides of Shibata with the peptides of Tenson to arrive at the method of the instant claims.

Since the combined disclosures of Shibata, Noaln, Daniels, and Tenson provide no reason for one skilled in the art to use peptides of 2 to 8 amino acids in length in a method of the instant claims with a reasonable expectation that these peptides would be capable of restoring or modifying the function of the wild type and/or mutant p53, the instant claims cannot be obvious over these references.

Finally, the Office asserts on page 10 of the Office Action that one skilled in the art would be motivated to use peptides of "various lengths" in the instantly claimed method because peptides of "various lengths" are disclosed in the art. First of all, the instant claims do not recite peptides of "various lengths"; instead, instant claims are directed to a method of identifying peptides of specific length, i.e., 2-8 amino acids. Second, there is nothing in the cited art giving reason to the one skilled in the art to use peptides of 2 to 8 amino acids to restore or modify the function of wild type and/or mutant p53. As recently reiterated in *Bayer Schering Pharma AG v. Barr Laboratories Inc.*, 91 USPQ2d 1569, 1573 (Fed. Cir. 2009), generalities or vague or non-existent guidance towards the claimed invention is insufficient to render a claim obvious; there must be some reason for the ordinary artisan to make the *particular* invention being claimed. The cited art provides no reason for one of ordinary skill in the art to use peptides of 2 to 8 amino acids in a method of the instant claims.

More importantly, however, it has surprisingly been found that very small peptides can restore or modify the function of target proteins through interacting with target proteins *in vivo* and altering their conformation (see p. Specification p. 4, ll. 16-24). These results and findings are not predictable from the cited art and are an independent reason as to why the instant claims are non-obvious.

For the foregoing reasons, Applicant respectfully submits that this obviousness rejection should be withdrawn because the Office has failed to make a *prima facie* case of obviousness for claims 38, 41, 42, 45, 48-51, 54 and 55 over Shibata, Noaln, Daniels, and Tenson alone or in combination.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Claims 38, 41, 42, 45, 48-51, 54 and 55 stand rejected under 35 USC §103(a) as being allegedly obvious over Shibata *et al.* (EP 0989136) ("Shibata"), Noaln *et al.* (WO 97/27212) ("Noaln"), Daniels *et al.* (J. Mol. Biol. Vol. 243:639-652; 1994) ("Daniels"), and if necessary, in view of Tenson *et al.* (J. Biol. Chem. Vol. 272(28): 17425-17430) ("Tenson"), and in further view of Thornborrow et al. (JBC Vol. 274(47): 33747-33756) ("Thornborrow"). Applicant respectfully traverses this rejection.

As stated above, the instant claims are not obvious over Shibata, Noaln, Daniels, and Tenson alone or in combination. Furthermore, as stated in the Response to the Office Action mailed March 12, 2009, the teachings of Thornborrow fail to cure the deficiencies of these references. Briefly, Thornborrow generally teaches p53-mediated transactivation of various promoters in different cells types. However, Thornborrow does not teach methods for screening peptide libraries. Furthermore, Thornborrow is silent on identifying peptides of 2-8 amino acids in length having the ability to restore the function of wild type and/or mutant p53 in an intra-cellular environment. Thus, one skilled in the art would not look to Thornborrow to supplement the method of Shibata to arrive at the instantly claimed method of identifying a peptide of 2-8 amino acids in length having the ability to restore the function of p53 in an intra-cellular environment.

Since the combined disclosures of Shibata, Noaln, Daniels, Tenson, and Thornborrow provide no reason for one skilled in the art to use peptides of 2 to 8 amino acids in length in a method of the instant claims with a reasonable expectation that these peptides would be capable of restoring or modifying the function of the wild type and/or mutant p53, the instant claims cannot be obvious over these references.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Claims 38, 41-45, 48-51, 54 and 55 stand rejected under 35 USC §103(a) as being allegedly obvious over Shibata *et al.* (EP 0989136) ("Shibata"), Noaln *et al.* (WO 97/27212) ("Noaln"), Daniels *et al.* (J. Mol. Biol. Vol. 243:639-652; 1994) ("Daniels"), and if necessary, in view of Tenson *et al.* (J. Biol. Chem. Vol. 272(28): 17425-17430) ("Tenson") and Thornborrow et al. (JBC Vol. 274(47): 33747-33756) ("Thornborrow"), and in further view of Skarnes (US 5,767,336) ("Skarnes"). Applicant respectfully traverses this rejection.

As stated above, the instant claims are not obvious over Shibata, Noaln, Daniels, Tenson, and Thornborrow alone or in combination. Furthermore, as stated in the Response to the Office Action mailed March 12, 2009, the teachings of Skarnes do not cure the deficiencies of these references. Briefly, Skarnes generally teaches vectors and reporter gene products including a secretion signal peptide or a transmembrane domain. However, Skarnes is silent on identifying peptides of 2-8 amino acids in length having the ability to restore the function of mutant p53 in an intra-cellular environment. One skilled in the art simply would not look to Skarnes to supplement the method of Shibata to arrive at the instantly claimed method of identifying a peptide of 2-8 amino acids in length having the ability to restore the function of p53 in an intra-cellular environment.

Since the combined disclosures of Shibata, Noaln, Daniels, Tenson, Thornborrow, and Skarnes provide no reason for one skilled in the art to use peptides of 2 to 8 amino acids in length in a method of the instant claims with a reasonable expectation that these peptides would be capable of restoring or modifying the function of the wild type and/or mutant p53, the instant claims cannot be obvious over these references.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

The Applicant respectfully submits that in view of the foregoing arguments and amendments the claims are in condition for allowance, which the Applicant respectfully requests. If the Examiner believes a teleconference will advance prosecution, he is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

Date: May 24, 2010

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